The following is a complete listing of all claims in the application, with an indication of the status of each:

Listing of claims:

1. (Currently amended) A method of detecting an interaction among agents in a group or mixture using a fixed- ratio ray design and determining whether subsets of said agents also interact, in order to detect, characterize or predict an outcome caused by exposure to said agents in said group or mixture, comprising the steps of

a) determining an additivity model from single chemical dose-response data for said agents in said mixture or group, wherein said single chemical dose-response data is obtained in test subjects;

b) fitting a mixture model in terms of total dose to mixture dose-response data from fixed-ratio rays for said agents in said group or mixture, wherein said mixture data is obtained in test subjects;

c) statistically comparing said additivity model to said mixture model to detect a departure from additivity, wherein a difference between said additivity model and said mixture model indicates an interaction among said agents in said group or mixture;

d) removing at least one subset of agents from said group or mixture, wherein relative ratios of amounts of remaining agents stay the same as in said fixed-ratio ray design such that $\frac{a_{i(full)}}{a_{j(full)}} = \frac{a_{i(reduced)}}{a_{j(reduced)}}$ where $a_{i(full)}$ is a proportion of the i^{th} chemical in said group or mixture, $a_{j(full)}$ is a proportion of the j^{th} chemical in said group or mixture, $a_{i(reduced)}$ is a proportion of the i^{th} chemical in said remaining agents, and $a_{j(reduced)}$ is the proportion of the j^{th} chemical in said remaining agents;

e) repeating steps b and c for agents remaining in said group or mixture after removal of said subset; and

f) determining whether or not said remaining agents interact with said subset of agents by utilizing statistical hypothesis testing using said full and reduced ray mixture models, in order to detect, characterize or predict an outcome caused by exposure to said agents in said group or mixture; and

g) providing results obtained in step f in the form of a plot or table.

2. (Original) The method of claim 1 wherein said method is applied to a plurality of full-ray groups.

3. (Original) The method of claim 1 further comprising the step of carrying out steps b and c for said subset of agents.

4. (Original) The method of claim 1, wherein said additivity model is graphically represented as an additivity curve and said mixture model is graphically represented as a mixture curve in terms of total dose.

5. (Original) The method of claim 1, further comprising the step of determining simultaneous confidence bands on the difference between said additivity curve and said mixture curve or between mixture curves on full and reduced rays.

6. (Currently amended) A method of detecting, in a group or mixture of agents, using a fixed-ratio ray design, the number of agents that interact, and determining whether subsets of said agents also interact, in order to detect, characterize or predict an outcome caused by exposure to said agents in said group or mixture, comprising the steps of

a) fitting a suitable polynomial in total dose to experimental dose-response data obtained with a combination of said agents said experimental data is obtained in test subjects;

b) statistically identifying higher order terms of said polynomial that are not equal to zero, wherein the number of agents that interact in said group or mixture of agents is equal to the degree of said higher order terms that are not equal to zero;

c) removing at least one subset of agents from said group or mixture, wherein relative ratios of amounts of remaining agents stay the same as in said fixed-ratio ray design such that $\frac{a_{i(full)}}{a_{j(full)}} = \frac{a_{i(reduced)}}{a_{j(reduced)}}$ where $a_{i(full)}$ is a proportion of the i^{th} chemical in said group or mixture,

$a_{i(full)}$ is a proportion of the j^{th} chemical in said group or mixture, $a_{i(reduced)}$ is a proportion of the i^{th} chemical in said remaining agents, and $a_{i(reduced)}$ is the proportion of the j^{th} chemical in said remaining agents;

d) repeating steps a and b for agents remaining in said group or mixture after removal of said subset;

e) determining whether or not said remaining agents interact with said subset of agents by utilizing statistical hypothesis testing using said full and reduced ray mixture models, in order to detect, characterize or predict an outcome caused by exposure to said agents in said group or mixture; and

f) providing results obtained in step e in the form of a plot or table.

7. (Original) The method of claim 6 wherein said method is applied to a plurality of full-ray groups.

8. (Original) The method of claim 6 further comprising the step of carrying out steps a and b for said subset of agents.

9. (Original) The method of claim 6, wherein single chemical data are used to estimate an additivity model which is linked to a linear term in said polynomial model.

10. (Original) The method of claim 9, wherein an additivity model is graphically represented as an additivity curve and said polynomial model is graphically represented as a mixture curve in terms of total dose.

11. (Original) The method of claim 6, wherein said polynomial is embedded in a generalized linear model.

12. (Original) The method of claim 6, wherein said polynomial is embedded in a general non-linear model.

13. (Original) The method of claim 6, further comprising the step of generating a graphical representation of said polynomial in total dose.

14. (Currently amended) A method of determining an interaction threshold boundary for agents in a group or mixture in order to detect, characterize or predict an outcome caused by exposure to said agents in said group or mixture, comprising the steps of

generating, ~~from fixed ratio ray data,~~ a generalized linear model or general nonlinear model that permits estimation of the boundaries between a region of additivity of said agents and a region of interaction of said agents, wherein said generalized linear model and said general nonlinear model are represented by

$$g(\mu)=\begin{Bmatrix} \beta_0+\sum_{r=1}^{c}\beta_r x_r, & x_c \le Q(x_1,x_2,...,x_{c-1}) \\ \beta_0+\sum_{r=1}^{c}\beta_r x_r+\sum_{r=1}^{c-1}\sum_{s=r+1}^{c}\beta_{rs}x_r x_s+ & \\ \sum_{r=1}^{c-2}\sum_{s=r+1}^{c-1}\sum_{u=s+1}^{c}\beta_{rsu}x_r x_s x_u+ & x_c > Q(x_1,x_2,...,x_{c-1}) \\ ...+\beta_{12...c}x_1x_2...x_c & \end{Bmatrix}$$

or by

$$\begin{Bmatrix} \beta_0+\sum_{r=1}^{c}\beta_r x_r, & x_c \le Q(x_1,x_2,...,x_{c-1}) \\ \beta_0+\sum_{r=1}^{c}\beta_r x_r+\sum_{r=1}^{c-1}\sum_{s=r+1}^{c}\beta_{rs}x_r x_s+ & \\ \sum_{r=1}^{c-2}\sum_{s=r+1}^{c-1}\sum_{u=s+1}^{c}\beta_{rsu}x_r x_s x_u+ & x_c > Q(x_1,x_2,...,x_{c-1}) \\ ...+\beta_{12...c}x_1x_2...x_c & \end{Bmatrix}$$

embedded in a general nonlinear model, respectively;

and said boundaries define said interaction threshold boundary, and

wherein said step of generating is carried out in order to detect, characterize or predict an outcome caused by exposure to said agents in said group or mixture; and

providing results obtained by said method in the form of a plot or table.

15. (Original) The method of claim 14, wherein said region of additivity of said agents and said region of interaction of said agents is determined by the steps of

a) determining an additivity model from single chemical data for said agents in said mixture or group, wherein said single chemical data is obtained in test subjects;

b) fitting an interaction threshold mixture model that incorporates an interaction threshold parameter in terms of total dose to mixture data from fixed-ratio rays for said agents in said group or mixture, wherein said mixture data is obtained in test subjects; and

c) statistically comparing said additivity model to said interaction threshold mixture model to detect a departure from additivity, wherein a region of difference between said additivity model and said interaction threshold mixture model indicates a region of interaction among said agents in said group or mixture, and a region of coincidence between said additivity model and said interaction threshold mixture model indicates a region of additivity among said agents in said group or mixture.

16. (Original) The method of claim 15 wherein said method is applied to a plurality of full-ray groups.

17. (Currently amended) The method of claim 15 further comprising the steps of

d) removing at least one subset of agents from said group or mixture wherein relative ratios of amounts of remaining agents stay the same as in said fixed-ratio ray design such that

$\frac{a_{i(full)}}{a_{j(full)}} = \frac{a_{i(reduced)}}{a_{j(reduced)}}$ where $a_{i(full)}$ is a proportion of the i^{th} chemical in said group or mixture, $a_{j(full)}$, is a proportion of the j^{th} chemical in said group or mixture, $a_{i(reduced)}$ is a proportion of the i^{th} chemical in a subset of remaining agents, and $a_{j(reduced)}$ is the proportion of the j^{th} chemical in said remaining agents;

e) repeating steps b and c for agents remaining in said group or mixture after removal of said subset; and

f) determining whether or not said remaining agents interact with said subset of agents by utilizing statistical methods based on algebraic manipulations relating full and reduced ray interaction threshold mixture models.

18. (Original) The method of claim 15 further comprising the step of carrying out steps b and c for said subset of agents.

19. (Original) The method of claim 14, wherein said region of additivity of said agents and said region of interaction of said agents is determined by the steps of

a) determining an additivity model from single chemical dose response data for said agents in said mixture or group, wherein said single chemical dose response data is obtained in test subjects;

b) fitting an interaction threshold mixture model that incorporates an interaction threshold parameter in terms of total dose to mixture data from fixed-ratio rays, wherein said region of additivity is conditioned on results obtained in step a; and

c) statistically comparing said additivity model to said interaction threshold mixture model to detect a departure from additivity, wherein a region of difference between said additivity model and said interaction threshold mixture model indicates a region of interaction among said agents in said group or mixture, and a region of coincidence between said additivity model and said interaction threshold mixture model indicates a region of additivity among said agents in said group or mixture.

20. (Original) The method of claim 19 wherein said method is applied to a plurality of full-ray groups.

21. (Currently amended) The method of claim 19 further comprising the steps of

d) removing at least one subset of agents from said group or mixture, wherein relative ratios of amounts of remaining agents stay the same as in said fixed-ratio ray design such that

$\frac{a_{i(full)}}{a_{j(full)}} = \frac{a_{i(reduced)}}{a_{j(reduced)}}$ where $a_{i(full)}$ is a proportion of the i^{th} chemical in said group or mixture, $a_{j(full)}$ is a proportion of the j^{th} chemical in said group or mixture, $a_{i(reduced)}$ is a proportion of the i^{th} chemical in said remaining agents, and $a_{j(reduced)}$ is the proportion of the j^{th} chemical in said remaining agents;

e) repeating steps b and c for agents remaining in said group or mixture after removal of said subset; and

f) determining whether or not said remaining agents interact with said subset of agents by utilizing statistical hypothesis testing using said full and reduced ray interaction threshold mixture models.

22. (Original) The method of claim 19 further comprising the step of carrying out steps b and c for said subset of agents.

23. (Original) The method of claim 14, wherein said region of additivity of said agents and said region of interaction of said agents is determined by the steps of

a) fitting an interaction threshold mixture model parameterized with a polynomial function for regions of interaction to experimental data obtained with a combination of said agents, wherein said experimental data is obtained in test subjects, and

b) statistically testing whether the interaction threshold parameter is different from zero and identifying higher order terms of said polynomial that are not equal to zero.

24. (Previously presented) The method of claim 23 wherein said method is applied to a plurality of full-ray groups or mixtures.

25. (Currently amended) The method of claim 23, further comprising the steps of

c) removing at least one subset of agents from said group or mixture wherein relative ratios of remaining agents stay the same as in said fixed-ratio ray design such that $\frac{a_{i(full)}}{a_{j(full)}} = \frac{a_{i(reduced)}}{a_{j(reduced)}}$.

where $a_{i(full)}$ is a proportion of the i^{th} chemical in said group or mixture, $a_{j(full)}$ is a proportion of the j^{th} chemical in said group or mixture, $a_{i(reduced)}$ is a proportion of the i^{th} chemical in said remaining agents, and $a_{j(reduced)}$ is the proportion of the j^{th} chemical in said remaining agents;

d) repeating steps a and b for agents remaining in said group or mixture after removal of said subset; and

e) determining whether or not said remaining agents interact with said subset of agents by utilizing statistical methods based on algebraic manipulations to compare full and reduced ray mixture models.

26. (Original) The method of claim 23, wherein single chemical data are also utilized, wherein said single chemical data is obtained in test subjects.

27-29 (Cancelled)

30. (Currently amended) Software for causing a computer to carry out a method of detecting an interaction among agents in a group or mixture using a fixed- ratio ray design and determining whether subsets of said agents also interact in order to detect, characterize or predict an outcome caused by exposure to said agents in said group or mixture wherein said method comprises the steps of

a) determining an additivity model from single chemical dose response data, wherein said single chemical dose response data is obtained in test subjects;

b) fitting a mixture model in terms of total dose to mixture data from fixed-ratio rays for said agents in said group or mixture, wherein said mixture data is obtained in test subjects;

c) statistically comparing said additivity model to said mixture model to detect a departure from additivity, wherein a difference between said additivity model and said mixture model indicates an interaction among said agents in said group or mixture;

d) removing at least one subset of agents from said group or mixture, wherein relative ratios of amounts of remaining agents stay the same as in said fixed-ratio ray design such that

$\frac{a_{i(full)}}{a_{j(full)}} = \frac{a_{i(reduced)}}{a_{j(reduced)}}$ where $a_{i(full)}$ is a proportion of the ith chemical in said group or mixture, $a_{j(full)}$ is a proportion of the jth chemical in said group or mixture, $a_{i(reduced)}$ is a proportion of the ith chemical in said remaining agents, and $a_{j(reduced)}$ is the proportion of the jth chemical in said remaining agents;

e) repeating steps b and c for agents remaining in said group or mixture after removal of said subset; and

f) determining whether or not said remaining agents interact with said subset of agents by utilizing statistical hypothesis testing using said full and reduced ray mixture models in order to detect, characterize or predict an outcome caused by exposure to said agents in said group or mixture; and

g) providing results obtained in step f in the form of a plot or table.

31. (Currently amended) Software for causing a computer to carry out a method of detecting, in a group or mixture of agents, using a fixed-ratio ray design, the number of agents that interact, and determining whether subsets of said agents also interact, in order to detect, characterize or predict an outcome caused by exposure to said agents in said group or mixture, wherein said method comprises the steps of

a) fitting a suitable polynomial in total dose to experimental data obtained with a combination of said agents wherein said experimental data is obtained in test subjects;

b) statistically identifying higher order terms of said polynomial that are not equal to zero, wherein the number of agents that interact in said group or mixture of agents is equal to the degree of said higher order terms that are not equal to zero;

c) removing at least one subset of agents from said group or mixture, wherein relative ratios of amounts of remaining agents stay the same as in said fixed-ratio ray design design such that

$\frac{a_{i(full)}}{a_{j(full)}} = \frac{a_{i(reduced)}}{a_{j(reduced)}}$ where $a_{i(full)}$ is a proportion of the ith chemical in said group or mixture, $a_{j(full)}$ is a proportion of the jth chemical in said group or mixture, $a_{i(reduced)}$ is a proportion of the ith

chemical in said remaining agents, and $a_{j(reduced)}$ is the proportion of the j^{th} chemical in said remaining agents;

d) repeating steps a and b for agents remaining in said group or mixture after removal of said subset;

e) determining whether or not said remaining agents interact with said subset of agents by utilizing statistical hypothesis testing using said full and reduced ray mixture models in order to detect, characterize or predict an outcome caused by exposure to said agents in said group or mixture; and

f) providing results obtained in step e in the form of a plot or table.

32-38. (Canceled)